Maternal and fetal tissue selenium loads in nulliparous ewes fed supranutritional and excessive selenium during mid- to late pregnancy

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Maternal and fetal tissue selenium loads in nulliparous ewes fed supranutritional and excessive selenium during mid- to late pregnancy[1,2]

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ABSTRACT: The objective was to describe the effects of dietary Se concentration and source on fetal and maternal Se load when fed to nulliparous ewes during mid- to late pregnancy. Pregnant, nulliparous ewes (n = 32; 45.6 ± 2.3 kg; 330 ± 17 d of age) were randomly assigned to treatment diets. Treatments were 3.5 μg of Se·kg of $BW^{-1}\cdot d^{-1}$ from the basal Se in the diet (C1X); 75 (S20X) and 350 (S100X) μg of Se·kg of $BW^{-1}\cdot d^{-1}$, with additional Se from supplemental sodium selenate; and 75 μg of Se·kg of $BW^{-1}\cdot d^{-1}$, with additional Se from naturally occurring Se-enriched wheat grain (W20X). Treatment diets were initiated at d 50 of pregnancy and continued until slaughter at d 134 ± 4 of pregnancy. Plasma samples were collected from the ewes immediately before treatments commenced and every 14 d for 70 d. At slaughter, plasma was collected from ewes and their fetuses. Ewes were randomly assigned to 1 of 8 consecutive slaughter days. Maternal and fetal LM, kidney, and liver samples were collected and stored. Tissue and plasma samples were analyzed for Se. Compared with other treatments, S100X resulted in the greatest maternal tissue and plasma Se loads ($P < 0.001$). However, based on the total amount of Se consumed during the treatment period, efficiency of Se loading was greatest for the W20X treatment. Compared with C1X and S20X, Se loading in fetal tissues and plasma was greater ($P < 0.01$) for S100X and W20X treatments. In S100X-treated ewes, maternal plasma Se increased rapidly from d 50 to 64 but remained unchanged thereafter. Maternal plasma Se increased steadily throughout the experiment in W20X and S20X ewes, but remained unchanged in C1X throughout the study. Sodium selenate fed at 350 μg of Se·kg of $BW^{-1}\cdot d^{-1}$ and Se-enriched wheat grain at 75 μg of Se·kg of $BW^{-1}\cdot d^{-1}$ to nulliparous pregnant ewes neither induced signs of selenosis nor negatively influenced ewe or fetal growth and development. Therefore, ewes in this study were capable of consuming greater than twice the current Se maximum tolerable limit as sodium selenate without experiencing selenosis. Selenium from Se-enriched wheat grain treatment seemed to cross the placenta to the fetus at greater efficiency than did Se from sodium selenate and was equivalent in Se-loading potential to sodium selenate-Se that was fed at nearly 5 times the amount of wheat grain Se.

Key words: fetus, pregnancy, selenium, selenomethionine, toxicity

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INTRODUCTION

The Se maximum tolerance concentration (**MTC**) for sheep was suggested to be 5.0 mg of Se·kg of DM^{-1} in the Nutrient Requirements for Small Ruminants (NRC, 2007). This was in accordance with the Mineral Tolerances of Animals (NRC, 2005) and the Se MTC increase from 2.0 (NRC, 1980) up to 5.0 mg of Se·kg of DM^{-1}. For a 40-kg yearling ewe, consumption of 5 mg of Se·kg of DM^{-1} feedstuffs equates to ≈160 μg of

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Se·kg of $BW^{-1}·d^{-1}$, but data indicate that sheep are capable of handling greater Se intakes. For example, ewes consuming ≈335 μg of Se·kg of $BW^{-1}·d^{-1}$ for 72 wk maintained expected productivity, and neither they nor their offspring demonstrated selenosis-related signs (Davis et al., 2006a,b). However, in addition to animal health, the 5.0 mg of Se·kg of DM^{-1} MTC was established when considering the possibility that excessive Se accumulation might occur in edible tissues. Therefore, more data are needed that addresses the effects of dietary Se fed beyond recommended requirements (NRC, 2007) and, especially, beyond the suggested MTC (NRC, 2005) on tissue Se load and corresponding livestock productivity.

Recently, Neville et al. (2008) described the effects of Se on growth and development of maternal and fetal tissues of pregnant ewe lambs. They found that Se fed at 75 and 350 μg·kg of $BW^{-1}·d^{-1}$ resulted in increased liver mass, decreased adrenal gland and blood masses, and increased proliferating cells of the jejunal mucosa. However, signs of selenosis were not detected. Since publication of these data, the Se content of the maternal and fetal tissues from that study have been analyzed, but not reported. These new data provide complementary Se load information to the effects reported in Neville et al. (2008). Therefore, the objective was to describe the effects of dietary Se concentration and source on fetal and maternal Se load when fed to nulliparous ewes during mid- to late pregnancy.

MATERIALS AND METHODS

The USDA, ARS, US Sheep Experiment Station (Dubois, ID) and North Dakota State University, Fargo, Institutional Animal Care and Use Committees reviewed and approved all animal-related procedures described herein.

Animal Care and Use

These data are the result of the same treatments that were applied to the same ewes as described in the work of Neville et al. (2008). In that publication, the authors summarized the effects of the Se treatments described below on the mass, growth, cellularity, and proliferation of maternal and fetal viscera, and vascularity of maternal jejunum in pregnant ewe lambs. We encourage readers to consult Neville et al. (2008) for experimental procedures and techniques not addressed herein.

Animals and Diet

Pregnant, Targhee, nulliparous ewes (n = 32; 45.6 ± 2.3 kg; 330 ± 17 d of age) were selected from a group of estrus-synchronized ewes (n = 80) that had been allowed to breed with rams for 4 d. Only ewes carrying single fetuses (transrectal ultrasound) at 30 d after the end of the breeding period were selected. For the purpose of convenience, the end of the breeding period is considered d 0 of pregnancy. Thus, from hereon, all times points (e.g., treatment commencement, sampling, slaughter) are in reference to d 0 of pregnancy. At d 45 of pregnancy, ewes were transported (1,500 km) from the USDA, ARS, US Sheep Experiment Station, Dubois, ID to North Dakota State University, Fargo; transport time was approximately 14.5 h. Upon arrival, ewes were moved to a ventilated, temperature-controlled (12°C), indoor facility with automated lighting (8-h daylight pattern). Ewes were weighed and placed in individual 0.9 × 1.2 m pens with water and salt provided for ad libitum intake. Ewes were fed a pelleted (0.48 cm) diet that consisted of 5% soyhulls, 33.5% sugar beet pulp, 2.5% soybean meal, 27% alfalfa meal, and 32% ground wheat grain (DM basis). Diet was formulated to contain 15.5% CP and 2.68 Mcal of ME/kg, DM basis, and was fed at a rate of 2.3% BW (DM basis) that was divided equally into 2 daily rations (fed at 0800 and 1600 h). The daily ration was adjusted according to BW, which was measured every 14 d, before the 0800 h feeding, throughout the experiment.

Treatments

To accomplish the experimental objectives, 4 dietary treatments were used in a complete randomized design. Ewes (n = 32) were randomly assigned to treatment. Treatments were 3.5 μg of Se·kg of $BW^{-1}·d^{-1}$ from the basal Se in the diet (**C1X**); 75 (**S20X**) and 350 (**S100X**) μg of Se·kg of $BW^{-1}·d^{-1}$, with additional Se from supplemental sodium selenate; and 75 μg of Se·kg of $BW^{-1}·d^{-1}$, with additional Se from naturally occurring Se-enriched wheat grain (**W20X**). Selenium treatment abbreviations, 1×, 20×, and 100×, signify 1-, 20-, and 100-fold, respectively, the approximate daily Se requirement for yearling ewes in late pregnancy (NRC, 2007). For referencing purposes, C1X, S20X, S100X, and W20X correspond to CONTROL, S3, S15, and SW treatment designations, respectively, in Neville et al. (2008).

Treatments were initiated on d 50 of pregnancy and continued until slaughter on d 134 ± 4 of pregnancy. For C1X, S20X, and S100X treatment diets, the wheat grain was harvested near Fargo, ND, and contained <0.2 μg of $Se·g^{-1}$ (DM basis). Wheat grain in the W20X treatment diet was harvested near Pierre, SD, and contained ≈9 μg of $Se·g^{-1}$ (DM basis). For S20X and S100X treatments, sodium selenate (source of Se) was dissolved in 10 to 15 mL of water and applied as a liquid top-dress once daily at the 0800 h feeding.

Sample Collection and Analyses

Plasma samples (from 8 mL of blood collected via jugular venipuncture; EDTA anticoagulant; 1,500 × *g*, 28 min; stored at −20°C) were collected from the ewes immediately before treatments commenced and every 14 d for 70 d. Ewes were randomly assigned to 1 of 8 consecutive slaughter days, which ranged from d 130

to 138 of pregnancy. Immediately before euthanasia, a final plasma sample (described above) was collected from the ewes. Euthanasia consisted of captive-bolt stunning (directly behind the poll) with subsequent exsanguination via complete severing of the left and right carotid arteries and jugular veins. Longissimus muscle, kidney, and liver samples (≈5 g) were collected from ewes and fetuses, wrapped in foil, frozen (super-cooled in isopentane and submerged in liquid nitrogen), and stored at −80°C. Kidney and liver weights were measured. Plasma samples from 6 mL of whole blood (handled as described above) were collected from the fetuses via cardiopulmonary puncture.

Ewe plasma was analyzed for Se via inductively coupled plasma mass spectrometry as described elsewhere (Taylor, 2005; minimum detection limit = 10 ng/mL; interassay CV = 2.2% and intraassay CV = 3.5%; Utah State Veterinary Diagnostic Laboratory, Logan). Ewe and fetal tissues, and fetal plasma were analyzed for Se via hydride atomic absorption spectrometry as described elsewhere (Finley et al., 1996; minimum detection limit = 1 ng/g; interassay CV = 6.8% and intraassay CV = 9.5%; North Dakota State University, Fargo).

Statistical Analyses and Calculations

Data were subjected to various analyses (described below; SAS Inst. Inc., Cary, NC). The experimental design was a complete randomized design with ewe as the experimental unit.

Ewe plasma Se data were treated as repeated measures and analyzed using mixed models. The model included treatment, sampling day, and the treatment × day interaction as fixed effects. Because of unequal variances within sample day, heterogeneous autoregressive order one [arh(1), SAS Inst. Inc.] covariance structure was specified. Fixed effects were considered significant when the probability of a greater F was <0.05. The treatment × day interaction was significant. Therefore, least squares means differences within sampling day were determined using pairwise t-test comparisons with $\alpha \leq 0.05$. Linear regression analysis was used to determine rates of Se change in plasma within treatment across sampling day. Based on previous work (Taylor, 2005), plasma Se reached near maximal concentration in response to supranutritional-Se diets within the first 14 d of treatment. Therefore, initial (rate) responses of plasma Se over time (rate) to treatments were considered to occur between d 50 and 64 of pregnancy.

For maternal and fetal liver, kidney, and muscle Se data and fetal plasma Se data, homogeneity of variances were assessed using Levene's test. All tests were significant ($P < 0.05$), and thus data were analyzed using mixed models with the Satterthwaite approximation option (SAS) and an unequal variance model specified. The model included treatment as a fixed effect. Treatment effects were considered significant when the probability of a greater F was <0.05. When treatment effects were detected, least squares means differences were determined using the Tukey method for pairwise comparisons with $\alpha \leq 0.05$.

To demonstrate the influence of chemical form of Se on Se retention in pregnant ewes, a partial Se retention-efficiency percentage was calculated for each ewe as follows:

$$[(\text{Se load}_n - \text{Se load}_{\text{C1X}})/(\text{Se consumed}_n - \text{Se consumed}_{\text{C1X}})],$$

where Se load$_n$ = estimated amount of Se in liver, kidney, muscle, and plasma for n ewe at slaughter for treatments S20X, W20X, or S100X; Se load$_{\text{C1X}}$ = arithmetic average of the estimated amount of Se in liver, kidney, muscle, and plasma for a C1X ewe at slaughter; Se consumed$_n$ = total Se consumed during the treatment period for n ewe in treatments S20X, W20X, or S100X; and Se consumed$_{\text{C1X}}$ = arithmetic average of total Se that a C1X ewe consumed during the treatment period. Muscle mass was estimated as 40% of the empty BW at slaughter (Neville et al., 2008). Plasma mass was estimated as 55% of whole blood mass at slaughter (Neville et al., 2008). Ultimately, the liver, kidney, muscle, and plasma masses used for the calculation represented approximately 42% of the total body mass. The resulting percentage demonstrates the proportion of apparent Se retained in ewes after consuming different sources of Se at concentrations 20- to 100-fold requirements (NRC, 2007) during mid- to late pregnancy. The retention-efficiency percentages for the Se treatments were analyzed using an ANOVA. The model included treatment as a fixed effect. Treatment effects were considered significant when the probability of a greater F was <0.05. When treatment effects were detected, least squares means differences were determined using the Tukey method for pairwise comparisons with $\alpha \leq 0.05$.

RESULTS

Mid- to Late Pregnancy Plasma Se

Effects of Se source on ewe plasma during mid- to late pregnancy are presented in Figure 1. A treatment × sampling day interaction was detected ($P < 0.001$) for plasma Se. On d 50 of pregnancy, before treatments were initiated, ewe plasma Se was greater ($P = 0.05$) in S100X than S20X ewes; however, the magnitude of difference was only 1.1-fold. Compared with S20X ewes, plasma Se in C1X was similar ($P = 0.06$ to 0.46) from d 62 to 120 of pregnancy, but less ($P = 0.04$) on d 134. Compared with W20X ewes, plasma Se in C1X was similar ($P = 0.36$) on d 62 of pregnancy, but less ($P < 0.01$) on all other days. Ewe plasma Se was similar ($P = 0.36$ to 0.85) between S20X and W20X ewes on all sampling days. Plasma Se was greatest ($P < 0.001$) in S100X ewes on d 64 to 134 of pregnancy.

Initial rate of Se increase in plasma from d 50 to 64 of pregnancy in S20X, S100X, and W20X ewes was 6.2,

77.1, and 7.7 ng·mL^{-1}·d^{-1}, respectively. Plasma Se in S20X and W20X ewes increased linearly ($P < 0.05$) from d 64 to 134 of pregnancy at a rate 1.77 and 2.45 ng·mL^{-1}·d^{-1}, respectively, with apparent maximal concentration occurring at d 92. However, plasma Se (rate) in S100X treated ewes did not change ($P = 0.78$) during this same period, with apparent maximal concentrations occurring at d 64 of pregnancy. From d 50 to 134 of pregnancy, plasma Se (rate) in C1X ewes remained the same ($P = 0.65$).

Maternal and Fetal Tissue Se

Effects of Se source on maternal and fetal liver, kidney, and muscle Se, and fetal plasma Se at slaughter are presented in Table 1. Maternal liver Se concentrations (μg·g^{-1}) and contents (g) were greatest ($P < 0.02$) in S100X, least ($P < 0.005$) in C1X, and similar ($P = 0.08$ to 0.54) between S20X and W20X ewes. Fetal liver Se concentrations and contents were greater ($P < 0.05$) in W20X than in C1X and S20X ewes, greater ($P < 0.05$) in S100X than C1X ewes, similar ($P = 0.08$) between W20X and S100X ewes, and similar ($P = 0.84$ to 0.99) between C1X and S20X ewes. Treatment influenced neither maternal nor fetal liver weights ($P = 0.52$ and 0.07; grand means = 1,027 and 133.5 g; SEM = 25 and 7.3 g, respectively).

Maternal kidney Se concentrations and contents were greatest ($P < 0.006$) in S100X ewes, intermediate ($P < 0.01$) in and similar ($P = 0.63$ to 0.94) between W20X and S20X ewes, and least ($P < 0.05$) in C1X ewes. Fetal kidney Se concentration was greater ($P < 0.001$) in S100X and W20X ewes than in S20X and C1X ewes, similar ($P = 0.97$) between S100X and W20X ewes, and similar ($P = 0.96$) between S20X and C1X ewes. Treatment did not influence the total content of Se in fetal kidney tissue ($P = 0.16$; grand mean = 0.028 mg; SEM = 0.002 mg). Treatment influenced neither maternal nor fetal kidney weights ($P = 0.90$ and 0.28; grand means = 140.0 and 24.8 g; SEM = 3.0 and 1.3 g, respectively).

Maternal muscle Se concentration was greater ($P < 0.001$) in S100X and W20X ewes than in S20X and C1X ewes, similar ($P = 0.50$) between S100X and W20X ewes, and similar ($P = 0.11$) between S20X and C1X ewes. Fetal muscle Se concentration was greater ($P < 0.001$) in S100X and W20X ewes than in S20X and C1X ewes, similar ($P = 0.14$) between S100X and W20X ewes, and greater ($P < 0.001$) in S20X than in C1X ewes.

Fetal plasma Se concentration was similar ($P = 0.37$) between W20X and S100X ewes. Fetal plasma Se concentrations in treatment groups W20X and S100X were greater ($P < 0.001$) than S20X and C1X, and S20X was greater ($P < 0.001$) than C1X.

The apparent Se retention-efficiency percentage was greatest ($P < 0.001$) in W20X ewes and similar ($P = 0.90$) between S20X and S100X ewes. The Se retention-efficiency percentages for W20X, S20X, and S100X were 6.4, 2.1, and 1.9 ± 0.42%, respectively.

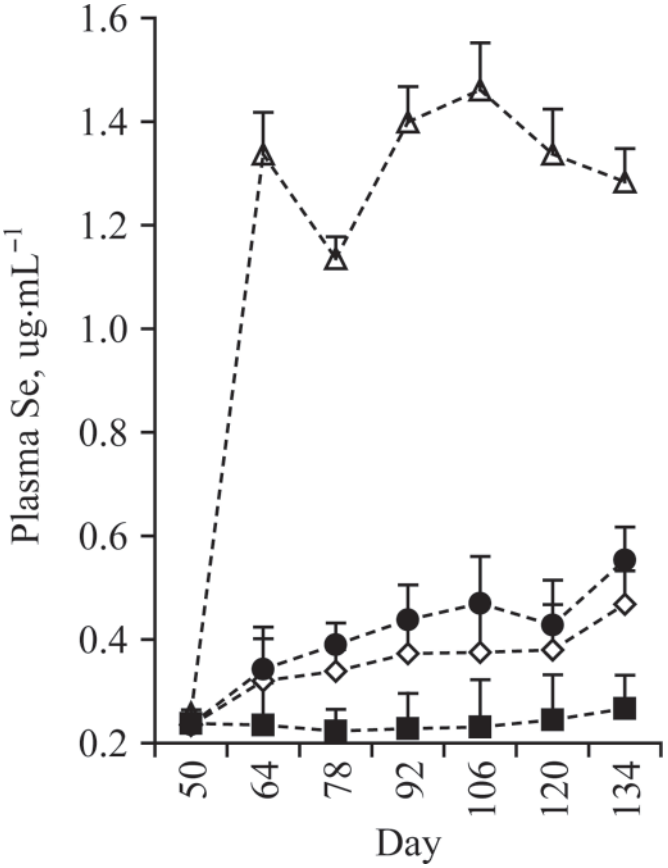

Figure 1. Plasma Se (least squares means with SEM as bars) concentrations in pregnant nulliparous ewes (age <1 yr) fed 3.5 μg of Se·kg of BW^{-1}·d^{-1} from the basal Se in the diet (■; C1X); 75 (◊; S20X) and 350 (Δ; S100X) μg of Se·kg of BW^{-1}·d^{-1}, with additional Se from supplemental sodium selenate; and 75 μg of Se·kg of BW^{-1}·d^{-1}, with additional Se from naturally occurring Se-enriched wheat grain (●; W20X) from d 50 to 134 of pregnancy.

DISCUSSION

Efficiency of Loading Maternal Tissues with Se

Selenium load in maternal tissues was increased when Se was fed at 20- to 100-fold the suggested requirement (NRC, 2007) to nulliparous ewe lambs during mid- to late pregnancy. Overall, the S100X treatment resulted in the greatest tissue Se loads in ewe maternal tissues except for the muscle. However, the efficiency of Se-loading in S100X ewes was less than in W20X ewes. Based on the partial Se retention-efficiency percentage, W20X treatment resulted in ≈3-fold (6.4% vs. 2.1 and 1.9%) more Se that was apparently retained in the liver, kidney, muscle, and plasma of pregnant ewes than the S20X and S100X treatments. This observation is consistent with other studies in which excessive (Davis et al., 2008) and toxic (Tiwary et al., 2006) amounts of organically bound Se resulted in greater whole-body loads in sheep than sodium selenite-Se. Therefore, Se-

Table 1. Least squares means (SEM) of tissue[1] Se concentrations (per unit; as-is basis) and contents (total) at d 134 ± 4 of pregnancy in nulliparous ewes (age <1 yr) fed 3.5 μg of Se·kg of $BW^{-1}\cdot d^{-1}$ from the basal Se in the diet (C1X); 75 (S20X) and 350 (S100X) μg of Se·kg of $BW^{-1}\cdot d^{-1}$, with additional Se from supplemental sodium selenate; and 75 μg of Se·kg of $BW^{-1}\cdot d^{-1}$, with additional Se from naturally occurring Se-enriched wheat grain (W20X) from d 50 to 134 of pregnancy

	Se treatment group[2]			
Item[3]	C1X	S20X	W20X	S100X
Maternal liver Se				
$\mu g\cdot g^{-1}$	0.56^{c} (0.09)	3.9^{b} (0.8)	5.9^{b} (1.0)	15.9^{a} (2.9)
mg	0.52^{c} (0.06)	4.1^{b} (1.0)	6.1^{b} (1.1)	17.5^{a} (3.7)
Fetal liver Se				
$\mu g\cdot g^{-1}$	0.56^{c} (0.04)	0.88^{bc} (0.10)	2.90^{a} (0.39)	3.09^{ab} (0.81)
mg	0.08^{c} (0.01)	0.11^{bc} (0.01)	0.34^{a} (0.06)	0.46^{ab} (0.13)
Maternal kidney Se				
$\mu g\cdot g^{-1}$	2.1^{c} (0.1)	3.4^{b} (0.22)	3.2^{b} (0.14)	5.5^{a} (0.55)
mg	0.28^{c} (0.01)	0.47^{b} (0.04)	0.46^{b} (0.02)	0.75^{a} (0.07)
Fetal kidney Se				
$\mu g\cdot g^{-1}$	0.84^{b} (0.13)	0.90^{b} (0.05)	1.34^{a} (0.11)	1.43^{a} (0.12)
mg	0.025 (0.005)	0.022 (0.003)	0.030 (0.003)	0.036 (0.006)
Maternal muscle Se[4]				
$\mu g\cdot g^{-1}$	0.27^{b} (0.03)	0.40^{b} (0.05)	0.91^{a} (0.06)	0.78^{a} (0.06)
Fetal muscle Se[4]				
$\mu g\cdot g^{-1}$	0.19^{c} (0.01)	0.26^{b} (0.01)	0.82^{a} (0.06)	0.59^{a} (0.07)
Fetal plasma Se				
$\mu g\cdot mL^{-1}$	0.12^{c} (0.005)	0.18^{b} (0.009)	0.33^{a} (0.007)	0.37^{a} (0.02)

[a–c]Within a row, different superscripts indicate a difference as determined using the Tukey's method for pairwise comparisons with $\alpha = 0.05$.
[1]Tissues were collected from ewes that were randomly assigned to 1 of 8 slaughter days from d 130 to 138 of pregnancy.
[2]n = 8 ewes/treatment.
[3]Treatment effects ($P < 0.05$) were detected for all response variables.
[4]Samples from LM.

enriched wheat grain, not sodium selenate, resulted in a greater proportional Se loading in maternal tissues of pregnant ewe lambs.

Se-Loading Potential of Treatments

The greater Se-loading potential of natural Se-enriched feeds seems to be because of the biochemical similarity between (*S*)-2-amino-4-(methylseleno)butyric acid (i.e., selenomethionine) and methionine. The predominant chemical form of Se in Se-enriched feeds, including yeast, is selenomethionine (Wu et al., 1997; Whanger, 2002). It is interchangeable with methionine during translation (Waschulewski and Sunde, 1988; Butler et al., 1989), but the aminoacylation of methionine is slightly favored over selenomethionine (Hoffman et al., 1970; McConnell and Hoffman, 1972). Because of this unique interchangeability, selenomethionine-Se is sequestered as a methionine-like compound away from Se-specific metabolism.

A methionine-like effect on Se loading is demonstrated when comparing Se concentrations in fetal and maternal tissues and changes in maternal plasma Se over time. Maternal liver, kidney, and plasma Se concentrations were different between W20X and S100X treatments, but in fetal tissues from the same ewes, the differences did not exist (d 134 of pregnancy). This suggests that more Se from Se-enriched wheat grain is transported across the placenta than Se from sodium selenate. But was the placenta capable of recognizing selenomethionine-Se as it did the sodium selenate-Se? Most likely, this is not the case. For example, the mean total Se in the liver of S20X-treated ewes was 7.9-fold the C1X mean, but in the fetal liver, the S20X mean total Se was only 1.4-fold the C1X mean. However, when comparing W20X and C1X treatments, the same calculated ratios are 11.7- and 4.3-fold, respectively. Taken together, these data suggest that the placenta is regulating Se transported to the fetus when sodium selenate and not a selenomethionine-rich feed was fed. In other words, if selenomethionine is functioning as methionine, then Se is being moved across the placenta through an AA transporter rather than Se-selective transporters. Thus, when selenomethionine-rich feeds are fed to pregnant sheep, Se loads in fetal tissue should parallel Se loads in maternal tissues (Hawkes et al., 1994).

Theoretically, the release of Se from the selenomethionine pool would be subject to the rate of methionine catabolism. By contrast, Se from sodium selenate arrives in the duodenum as completely reduced insoluble Se, partially reduced soluble Se (e.g., selenite), or as microbial-synthesized selenocysteine (van Ryssen et al., 1989). Selenocysteine does not replace cysteine during mammalian mRNA translation, and as with sodium selenate/selenite, is rapidly catabolized, and the Se is liberated as selenide (Esaki et al., 1982; Hasegawa et al., 1996; Nakamuro et al., 2000). The whole-body biological half-life of ^{75}Se from [^{75}Se]selenomethionine in

human females was 2.7 times more than ^{75}Se from [^{75}Se] selenite (Griffiths et al., 1976). Therefore, the methionine-like metabolic fate of selenomethioinine, which includes inadvertent Se transport and greater Se half-life, describes why all selenomethionine-rich feeds, including Se-enriched yeast, result in greater tissue Se-loading potential and efficiency than do traditional sodium selenate/selenite supplemental feeds.

Risks of Se Loading in Pregnant Ewes

Considering the magnitude of Se loading that occurred in the present study, it is important to establish whether S100X and W20X treatments did or did not negatively impact the pregnant ewes. As previously mentioned, these data are the unreported part of the published work of Neville et al. (2008). They summarized the effects of C1X, S20X, S100X, and W20X treatments on the mass, growth, cellularity, and proliferation of maternal and fetal viscera, and the vascularity of maternal jejunum in pregnant ewe lambs. Briefly, compared with the control group (orthogonal contrast = C1X vs. S20X + S100X + W20X0), Se treatment resulted in decreased maternal adrenal gland and blood masses, increased maternal liver mass (g·kg of BW^{-1}) and total liver protein, and increased total proliferating cells in fetal jejunal mucosa. But, neither did these effects seem negative, nor were signs of selenosis detected. Therefore, these results indicate that, regardless of the magnitude of tissue Se loading and alterations of some maternal and fetal tissues, Se fed at 350 μg of Se·kg of BW^{-1} as sodium selenate or 75 μg of Se·kg of BW^{-1} Se-enriched wheat grain to pregnant ewe lambs was not detrimental to pregnant ewes or their fetuses.

Dietary Se Beyond the Suggested MTC

Based on the present data and work of others (Davis et al., 2006a,b), adolescent and mature ewes can consume significantly more Se than the current suggested MTC of 5 mg of Se·kg of DM^{-1}·d^{-1} (≈160 μg of Se·kg of BW^{-1}·d^{-1}; NRC, 2005, 2007) without experiencing symptoms of selenosis or loss of productivity. However, data are not available that define what the exact MTC is for production ewes; that is beyond the scope of the present study. The initial (d 50 to 64 of pregnancy) rate of Se increase in plasma was greatest in S100X ewes (≈10-fold S20X and W20X), but from d 64 to 134 of pregnancy, there was no net rate change in S100X plasma Se. Plasma Se continued to increase in W20X and S20X treatments, with the greater rate of change occurring in W20X ewes. The differences in the plasma Se response between S20X and S100X may indicate a possible change in ability of tissues to metabolize and cope with excessive Se loads. In a linear fashion, BW gain lessened and, ultimately, BW decreased in mature wethers fed increasing concentrations of Se beginning at 3 (requirement) and increasing to ≈300 and 600 μg·kg of BW^{-1}·d^{-1} (Davis et al., 2008). However, no classical signs of selenosis were reported for the wethers. Evidence from the present study indicate that excessive Se intakes near or exceeding 350 μg of Se·kg of BW^{-1}·d^{-1} were tolerable (i.e., not a MTC) when fed to ewes from d 50 to 134 of pregnancy. But, based on and the literature (Davis et al., 2008), antiproductive consequences in sheep could be expected if such intakes are continued long-term.

Selenomethionine-Rich Feeds and Sheep Productivity

Feeding supranutritional Se as Se-enriched wheat grain (W20X) resulted in more Se being transferred to skeletal muscle of pregnant ewes than did sodium selenate treatments. This effect is consistent with the results of previous studies with sheep (van Ryssen et al., 1989; Davis et al., 2008), steers (Lawler et al., 2004), and rats (Taylor et al., 2005). Unique to this study was that sodium selenate-Se had to be fed at nearly 5 times the amount of wheat grain-Se to achieve similar maternal and fetal muscle Se concentrations. This increased bioavailability, combined with the long whole-body half-life of selenomethionine, makes selenomethionine-rich feed sources attractive alternatives to traditional Se salt supplements.

It is important to decipher whether selenomethionine-rich feeds, including Se-enriched yeast, are safer than traditional Se-salt supplements. Under subacute exposure (7 d), selenosis was detected in lambs at 2,000 and 4,000 μg of Se·kg of BW^{-1}·d^{-1} when Se was dosed as sodium selenite and selenomethionine, respectively (Tiwary et al., 2006). No ill effects of Se were observed at lesser doses. These data are consistent with assumptions that selenomethionine may be less toxic than sodium selenite. However, data are available that indicate that under chronic exposure this may not be so. For example, rats fed supranutritional Se as selenomethionine throughout the entire pregnancy had fewer fetuses compared with rats fed selenocystine (Taylor et al., 2005). More relevant to the current study, mature wethers that were consuming ≈425 and 562 μg of Se·kg of BW^{-1}·d^{-1} as Se-enriched yeast lost BW over 420 d, but wethers consuming no supplemental Se or the same concentrations of Se as sodium selenite gained BW (Davis et al., 2008). It seems that under chronic exposure conditions supplemental selenomethionine beyond the current Se MTC may negatively influence certain aspects of sheep production that would not necessary be affected if sodium selenite/selenate was fed.

In the context of sheep production, the information concerning selenomethionine and selenomethionine-rich feeds is important. Because of the rapid loading potential (Taylor, 2005; Tiwary et al., 2006) and extended half-life of selenomethionine (Griffiths et al., 1976; Hawkes et al., 1994), selenomethionine-rich feeds can be used to rapidly load ewes and their fetuses or nursing offspring with Se before they are moved to remote Se-deficient ranges for extended periods of time.

Because the potential for acute and subacute toxicity is much less for selenomethionine than it is for sodium selenite (Tiwary et al., 2006), episodes of selenosis are less likely when supranutritional Se is fed as natural Se-enriched feedstuffs.

Concluding Remarks

In nulliparous pregnant ewe lambs, supranutritional Se from Se-enriched wheat grain resulted in greater maternal and fetal tissue and plasma Se loads seemed to cross the placenta to the fetus at greater efficiency than did sodium selenite and exceed the Se-loading potential of sodium selenate-Se in both maternal and fetal tissues. Sodium selenate fed at 350 μg of Se·kg of $BW^{-1}\cdot d^{-1}$ and Se-enriched wheat grain at 75 μg of Se·kg of $BW^{-1}\cdot d^{-1}$ to nulliparous pregnant ewe lambs neither induced symptoms of selenosis nor negatively affected ewe lamb or fetal growth and development (Neville et al., 2008). Based on the sodium selenate data, ewes in this study were capable of consuming greater than twice the current Se MTC (NRC, 2007). Finally, consistent with previous work (Lawler et al., 2004; Taylor, 2005), a natural Se-enriched feedstuff was effective at simultaneously enriching maternal and fetal muscle. Such enrichment could enable producers to graze ewes and offspring on Se-deficient ranges for extended periods without the need of Se supplementation and have available for market a Se-enriched meat product.

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